

Claims

1. A method for detecting a protein *in situ*, the method comprising contacting a cell expressed peptide tag fusion protein with a nucleic acid aptamer that recognizes the peptide tag with high affinity and forms a complex, and detecting the complex.
2. The method of claim 1, wherein said aptamer is selected from the group consisting of a single stranded DNA, double stranded DNA, hairpin DNA, single stranded RNA, double stranded RNA, hairpin RNA, protein nucleic acid aptamer or a hybrid combination thereof.
3. The method of claim 2, wherein said nucleic acid aptamer is double stranded DNA.
4. The method of claim 2, wherein said aptamer is chemically modified.
5. The method of claim 4, wherein said chemical modification is selected from the group consisting of reactive thiols, amines, cobalt or iron paramagnetic beads, fluorophores, quantum dots, peptides, metal chelating peptides or compounds, gold particles, simple or complex sugars, biotin and combinations thereof.
6. The method of claim 1, wherein said peptide tag is selected from the group consisting of a natural or engineered sequence of a virus, *archaebacteria*, eukaryotic and a prokaryotic organism.
7. The method of claim 6, wherein said peptide tag is a prokaryotic DNA binding protein.
8. The method of claim 7, wherein said prokaryotic DNA binding protein is selected from the group consisting of Lac repressor, Tet repressor, fructose repressor, purine repressor, galactose repressor, AraC repressor, MerR repressor, MarR repressor, BmrR repressor, QacR repressor and EmrR repressor.
9. The method of claim 6, wherein said peptide tag is modified by a modification selected from the group consisting of methylation, acetylation, phosphorylation, ADP-ribosylation, sumolation, ubiquitination, glycosylation and any combination thereof.

10. The method of claim 8, wherein said DNA binding protein is a Lac repressor.
11. The method of claim 1, wherein said cell is selected from the group consisting of *archeobacterial* cell, prokaryotic cell and eukaryotic cell.
12. The method of claim 11, wherein said cell is a eukaryotic cell.
13. The method of claim 12, wherein said cell is a mammalian cell.
14. The method of claim 1, wherein prior to contacting, said cell is fixed and permeabilized.
15. The method of claim 5, wherein detecting is done by immunofluorescence.
16. The method of claim 1, wherein detection of said complex is visualized in a sub-cellular and/or sub-nuclear location within said cell.
17. The method of claim 1, wherein said aptamer is provided bound to a nitrocellulose membrane.
18. The method of claim 1, wherein said aptamer is provided as a microarray on a substrate.
19. A method for detecting proteins *in situ* in a cell, the method comprising;
  - a) preparing a protein/peptide tag fusion vector;
  - b) transforming a cell with a);
  - c) contacting b) with a chemically modified nucleic acid aptamer, wherein said protein tag is recognized by said nucleic acid aptamer and forms a complex; and
  - d) detecting said complex.
20. The method of claim 19, wherein said aptamer is selected from the group consisting of a single stranded DNA, double stranded DNA, hairpin DNA, single stranded RNA, double stranded RNA, hairpin RNA, protein nucleic acid aptamer or a hybrid combination thereof.

21. The method of claim 20, wherein said nucleic acid aptamer is double stranded DNA.
22. The method of claim 19, wherein said chemical modification is selected from the group consisting of reactive thiols, amines, cobalt or iron paramagnetic beads, fluorophores, quantum dots, peptides, gold particles, metal chelating peptides or compounds, simple or complex sugars, biotin and combinations thereof.
23. The method of claim 19, wherein said peptide tag is selected from the group consisting of a natural or engineered sequence of a virus, *archaeobacteria*, eukaryotic organism and a prokaryotic organism.
24. The method of claim 23, wherein said peptide tag is a prokaryotic DNA binding protein.
25. The method of claim 22, wherein said prokaryotic DNA binding protein is selected from the group consisting of the Lac repressor, Tet repressor, fructose repressor, purine repressor, galactose repressor, AraC repressor, MerR repressor, MarR repressor, BmrR repressor, QacR repressor and EmrR repressor.
26. The method of claim 19, wherein said peptide tag is modified by a modification selected from the group consisting of methylation, acetylation, phosphorylation, ADP-ribosylation, sumolation, ubiquitination, glycosylation, hydroxylation and any combination thereof.
27. The method of claim 25, wherein said DNA binding protein is a Lac repressor.
28. The method of claim 19, wherein said cell is selected from the group consisting of *archeobacterial* cell, prokaryotic cell and eukaryotic cell.
29. The method of claim 28, wherein said cell is a eukaryotic cell.
30. The method of claim 29, wherein said cell is a mammalian cell.

31. The method of claim 19, wherein prior to step c), b) is fixed and permeabilized.
32. The method of claim 19, wherein said complex is detected in a sub-cellular and/or sub-nuclear structure.
33. The method of claim 19, wherein detection is done by immunofluorescence.
34. A method for the detection of one or more proteins and/or protein complexes *in situ*, the method comprising:
- contacting a transfected cell expressing a fusion protein comprising a prokaryotic DNA binding protein with a functionalized nucleic acid aptamer, wherein said prokaryotic DNA binding protein is recognized by said functionalized nucleic acid aptamer to form a complex, and detecting said complex.
35. The method of claim 34, wherein said nucleic acid aptamer is selected from the group consisting of a single stranded DNA, double stranded DNA, hairpin DNA, single stranded RNA, double stranded RNA, hairpin RNA, protein nucleic acid aptamer or a hybrid combination thereof.
36. The method of claim 35, wherein said nucleic acid aptamer is double stranded DNA.
37. The method of claim 35, wherein said functionalized nucleic acid aptamer is functionalized with a group selected from the group consisting of reactive thiols, amines, cobalt or iron paramagnetic beads, fluorophores, quantum dots, peptides, metal chelating peptides or compounds, simple or complex sugars, biotin and combinations thereof.
38. The method of claim 35, wherein said cell is selected from the group consisting of *archebacterial* cell, prokaryotic cell and eukaryotic cell.
39. The method of claim 38, wherein said cell is a eukaryotic cell.
40. The method of claim 39, wherein said cell is a mammalian cell.

41. A method for the detection and purification of one or more proteins and/or protein complexes, the method comprising:
- a) transforming a cell with a protein/peptide tag fusion vector;
  - b) culturing a) to express a fusion protein comprising a desired protein fused to a protein tag;
  - c) making a cellular extract from b);
  - d) contacting c) with a nucleic acid aptamer bound to a solid matrix or beads, wherein said protein tag is recognized by said nucleic acid aptamer to form a complex; and
  - e) purifying said complex from d).
42. The method of claim 41, wherein said nucleic acid aptamer is selected from a single stranded or double stranded DNA, RNA, protein nucleic acid aptamer or a hybrid combination thereof.
43. The method of claim 42, wherein said nucleic acid aptamer is a double stranded DNA aptamer wholely or in part.
44. The method of claim 35, wherein said nucleic acid aptamer is functionalized with a group selected from the group consisting of reactive thiols, amines, cobalt or iron paramagnetic beads, fluorophores, quantum dots, peptides, metal chelating peptides or compounds, simple or complex sugars, biotin and combinations thereof.
45. The method of claim 41, wherein said cell is selected from the group consisting of *archeobacterial* cell, prokaryotic cell and eukaryotic cell.
46. The method of claim 45, wherein said cell is a eukaryotic cell.
47. The method of claim 46, wherein said cell is a mammalian cell.
48. The method of claim 41, wherein said peptide tag is selected from the group consisting of a natural or engineered sequence of a virus, *archaeobacteria*, eukaryotic organism and a prokaryotic organism.

49. The method of claim 48, wherein said peptide tag is a prokaryotic DNA binding protein.
50. The method of claim 49, wherein said prokaryotic DNA binding protein is selected from the group consisting of the Lac repressor, Tet repressor, fructose repressor, purine repressor and galactose repressor.
51. The method of claim 49, wherein said peptide tag is modified by a modification selected from the group consisting of methylation, acetylation, phosphorylation, ADP-ribosylation, sumolation, ubiquitination, glycosylation, hydroxylation and any combination thereof.
52. The method of claim 41, wherein said aptamer is covalently bound to sepharose beads.
53. The method of claim 41, wherein said aptamer is coupled to a paramagnetic particle.
54. The method of any one of claims 1, 19, 34 or 41, wherein said method is used to purify endogenous proteins.